

CLAIM

What is claimed is:

5 1. A composition for administering paclitaxel comprising:

- a) paclitaxel or an analog thereof;
- b) a pharmaceutically acceptable surfactant;
- c) a pharmaceutically acceptable solvent; and
- d) a substituted cellulosic polymer.

10 2. The composition of claim 1 which is self-emulsifying.

3. The composition of claim 1 which is for oral administration.

4. The composition of claim 2 wherein said surfactant is selected from the group consisting of polyoxyl 40 hydrogenated castor oil, polyoxyl 35 hydrogenated castor oil, polyoxyethylene sorbitan fatty acid esters, poloxamers, VE-TPGS 1000, polyoxyethylene alkyl ethers, Solutol HS-15, Tagat TO, Peglicol 6-oleate, polyoxyethylene sterates, and saturated polyglycolized glycerides.

5 The composition of claim 4 wherein said surfactant is selected from the group consisting of polyoxyl 40 hydrogenated castor oil, polyoxyl 35 hydrogenated castor oil, polyoxyethylene sorbitan fatty acid esters, poloxamers, and VE-TPGS 1000.

20 6. The composition of claim 5 wherein said surfactant is a polyoxyl 40 hydrogenated castor oil or a polyoxyl 35 hydrogenated castor oil.

25 7 The composition of claim 2 wherein the weight ratio of paclitaxel to the surfactant (paclitaxel:surfactant) is from about 1:3 to about 1:20.

8 The composition of claim 7 wherein the weight ratio of paclitaxel to the surfactant (paclitaxel:surfactant) is from about 1:5 to about 1:10.

30 9. The composition of claim 2 wherein said solvent is selected from the group consisting of polyethylene glycol, propylene glycol, ethanol, glycerol, triacetin, glycofurool, propylene

carbonate, dimethyl acetamide, dimethyl isosorbide, N-methyl pyrrolidinone, and mixture thereof.

10. The composition of claim 9 wherein said solvent is selected from the group consisting of polyethylene glycol, propylene glycol, ethanol, and a mixture thereof.

5 11. The composition of claim 10 wherein said solvent is a mixture of ethanol and a polyethylene glycol consisting of polyethylene glycol 400.

12. The composition of claim 2 wherein the said substituted cellulosic polymer is selected from the group consisting of hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), hydroxyethylcellulose, methylcellulose, maltodextrin, and povidones.

10 13. The composition of claim 12 wherein the said substituted cellulosic polymer is selected from the group consisting hydroxypropyl methylcellulose, hydroxyethylcellulose, hydroxypropyl cellulose, and methylcellulose.

14 The composition of claim 13 wherein said substituted cellulosic polymer is hydroxypropyl methylcellulose.

15. The composition of claim 2 wherein said substituted cellulosic polymer and paclitaxel are present in a ratio of about 50:1 to about 0.1:1 by weight.

16. The composition of claim 15 wherein said substituted cellulosic polymer and paclitaxel are present in a ratio of about 10:1 to about 0.1:1 by weight.

17. The composition of claim 16 wherein said substituted cellulosic polymer and paclitaxel are present in a ratio of about 5:1 to about 0.5:1 by weight.

18. The composition of claim 2 wherein said substituted cellulosic polymer is substantially water-soluble.

19. The composition of claim 14 wherein the hydroxypropyl methylcellulose has about 15% to about 35% methoxyl substitution and about 3% to about 15% hydroxypropyl substitution.

25 20. The composition of claim 19 wherein the hydroxypropyl methylcellulose has about 19% to about 24% methoxyl substitution and about 7% to about 12% hydroxypropyl substitution.

21. The composition of claim 3 which is contained in a water-soluble capsule.

22. The composition of claim 21 wherein the substituted cellulosic polymer is present in the capsule wall.

30 23. The composition of claim 22 wherein the substituted cellulosic polymer constitutes from about 5% to 100% by weight of the capsule wall.

24. The composition of claim 23 wherein the substituted cellulosic polymer constitutes from about 5% to 100% by weight of the capsule wall.

25. The composition of claim 2 which further comprises a diglyceride.

26. The composition of claim 25 wherein the diglyceride contains fatty acids of a carbon chain having 8 to 22 carbons with 0 to 3 double bonds.

5 27. The composition of claim 26 wherein the diglyceride contains fatty acids of a carbon chain having 16 to 18 carbons with 1-2 double bonds.

28. The composition of claim 25 wherein the diglyceride is selected from the group consisting of diolein, dilinoleate, and a mixture thereof.

10 29. The composition of claim 25 which further comprises a monoglyceride.

30. The composition of claim 29 wherein the monoglyceride contains fatty acids of a carbon chain having 8 to 22 carbons with 0 to 3 double bonds.

31. The composition of claim 29 wherein the monoglycerides contains fatty acids of a carbon chain having 16 to 18 carbons with 1-2 double bonds.

32. The composition of claim 29 wherein the monoglyceride is selected from the group consisting of monoolein, monolinoleate, and a mixture thereof.

33. The composition of claim 29 wherein the ratio of diglyceride to monoglyceride (diglyceride:monoglyceride) by weight is from about 9:1 to about 6:4.

34. The composition of claim 2 wherein the paclitaxel is present in an amount of up to about 100 mg/gm.

20 35. The composition of claim 34 wherein the paclitaxel is present in an amount of from about 10 to about 80 mg/gm.

36. The composition of claim 35 wherein the paclitaxel is present in an amount of from about 30 to 70 mg/gm.

25 37. The composition of claim 36 wherein the paclitaxel is present in an amount of from about 40 mg/gm to about 65 mg/gm.

38. The composition of claim 1 wherein said surfactant is present in an amount from about 100 to about 700 mg/g.

39. The composition of claim 2 wherein said solvent is present in an amount from about 30 100 to about 700 mg/g.

40. The composition of claim 3 further comprising a P-glycoprotein inhibitor.

41. The composition of claim 40 wherein said P-glycoprotein inhibitor is selected from the group consisting of alginates, xanthan, gellan gum, CRK-1605, cyclosporin A, verapamil, tamoxifen, quinidine, valsopdar, SDZ PSC 833, GF120918 (GG918, GW0918), ketocomazole, Psoralens, sucroster-15, R101933, OC144-093, Erythromycin, azithromycin, 5 RS-33295-198, MS-209, XR9576, and phenothiazine.

42. The composition of claim 41 wherein said P-glycoprotein inhibitor is cyclosporin A.

43. The composition of claim 42 wherein said cyclosporin A in the composition is in an amount of from about 0.1 to about 20 mg/kg patient body weight.

44. The composition of claim 1 wherein the surfactant is selected from the group 10 consisting of polyoxyl 40 hydrogenated castor oil, polyoxyl 35 hydrogenated castor oil, polyoxyethylene sorbitan fatty acid esters, poloxamers, vitamin E-TPGS 1000, polyoxyethylene alkyl ethers, Solutol HS-15, Tagat TO, Peglicol 6-oleate, polyoxyethylene sterates, and saturated polyglycolized glycerides; and wherein the substituted cellulosic polymer is selected from the group consisting of hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), hydroxyethylcellulose, methylcellulose, maltodextrin, and povidones.

45. The composition of claim 44 wherein the surfactant is selected from the group 20 consisting of a polyoxyl 40 hydrogenated castor oil and a polyoxyl 35 hydrogenated castor oil; wherein the solvent is selected from the group consisting of polyethylene glycol, propylene glycol, ethanol, and a mixture thereof; and wherein the substituted cellulosic polymer is selected from the group consisting of hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxyethylcellulose, and methylcellulose.

46. The composition of claim 45 wherein the surfactant is a polyoxyl 35 hydrogenated castor oil; wherein the solvent is a mixture of polyethylene glycol ethanol; and wherein the substituted cellulosic polymer is hydroxypropyl methylcellulose.

47. The composition of claim 45 further comprising a diglyceride.

48. The composition of claim 47 wherein the diglyceride is glyceryl dioleate.

49. A method of treating a patient suffering from cancer and in need of treatment comprising administration to said patient a composition comprising:

30 a) a chemotherapeutically effective amount of paclitaxel,

b) a pharmaceutically acceptable surfactant,

c) a pharmaceutically acceptable solvent, and

d) a substituted cellulosic polymer.

50. The method of claim 49 wherein the amount of said paclitaxel in the composition is from about 10 to about 80 mg/g.

51. The method of claim 50 wherein the amount of said paclitaxel in the composition is from about 30 to about 70 mg/g.

52. The method of claim 51 wherein the amount of said paclitaxel in the composition is from about 40 to about 65 mg/g.

53. The method of claim 49 wherein said composition further comprises a diglyceride.

10 54. The method of claim 53 wherein said composition further comprises a mono-glyceride.

15 55. The method of claim 54 wherein the ratio of the diglyceride to monoglyceride, by weight, in the composition is from about 9 :1 to about 6:4.

20 56. The method of claim 53 wherein the composition is administered orally.

57. The method of claim 56 wherein the composition further comprises a P-glycoprotein inhibitor.

25 58. The method of claim 58 wherein said P-glycoprotein inhibitor is selected from the group consisting of cyclosporin A, verapamil, tamoxifen, quinidine, phenothiazene, and mixtures thereof. or related P-glycoprotein inhibitors.

59. The method of claim 57 wherein the amount of said P-glycoprotein inhibitor in the composition is from about 0.1 to about 20 mg/kg patient body weight.

60. The composition of claim 14 wherein the hydroxypropyl methylcellulose has a viscosity range of about 1 to 1 about 100,000 cps.

25 61. The composition of claim 60 wherein the hydroxypropyl methylcellulose has a viscosity range of about 1 to about 4,000 cps.

62. The composition of claim 14 wherein the hydroxypropyl methylcellulose is type 2208 or 2910.

30 63. The composition of claim 21 wherein the substituted cellulosic polymer is present in the fill liquid composition.

64. The composition of claim 1 which generates a supersaturated state upon dilution with water.